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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,845	10/18/2001	Fred Levine	02307O-110910US	7736

20350 7590 08/24/2004

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EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/041,845	LEVINE ET AL.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-15,17-21 and 31-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12-15,17-21 and 31-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed August 3, 2004. Amendments were made to the claims. Specifically, claim 16 was cancelled, and new claims 38-43 were added

Claims 1-10, 12-15, 17-21 and 31-43 are pending and under consideration in the instant application. Any rejection of record in the previous Office Action, mailed May 3, 2004, that is not addressed in this action has been withdrawn.

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

The following represents a non-final Office Action on the merits, concerning issues that were not previously raised in the prosecution.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 17, 31, 32 and 37-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Sharma (US 2003/0087394; see entire document; henceforth Sharma). **This is a new rejection that is not necessitated by amendment of the claims.**

Sharma teaches a method of treating a subject having an insulin related disease, using a cell that is induced to produce insulin (see for example paragraph [0092]). In order to practice the invention, one must first produce the cell to be used in the method. Sharma indicates that the origin of such a cell can be a human pancreatic β-cell, including pancreatic endocrine cells (see for example paragraph [0092]). In a preferred embodiment, the cell is also genetically modified to express (i.e., recombinantly) one or more genes that include both PDX-1 and NeuroD/BETA2 (see for example paragraph [0092]). Thus, Sharma anticipates a human endocrine pancreatic β-cell as set forth in the instant claims 31 and 32. Sharma further teaches that these cells can be cultured (see for example paragraph [0096]); absent evidence to the contrary, these insulin cells will be stimulated to produce insulin by the action of a GLP-1 agonist, given the natural mechanism of GLP-1 agonists on insulin producing cells. Furthermore, these cells will necessarily experience a level of cell-to-cell contact when being cultured (although this does not necessarily amount to the cells aggregating due to cell-to-cell contact), given the dynamic of culture systems. Thus, Sharma also anticipates the stable cultures of cells that are indicated in claims 17 and 37-40.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10, 12-15, 17-21 and 31-43 rejected under 35 U.S.C. 103(a) as being unpatentable over Sharma as applied to claims 17, 31, 32 and 37-40 under 35 USC § 102(e), in view of Levine (US 6,448,045; see entire document; henceforth Levine). **This is a new rejection that is not necessitated by the amendment of the claims.**

Sharma teaches all of the elements set forth above in the rejection of claims 17, 31, 32 and 37-40 under 35 USC § 102(e). Sharma further teaches a method of producing insulin (i.e., inducing insulin gene expression) in cells, including human endocrine pancreatic β-cells (see for example paragraphs [0107-0108]). Sharma teaches that these cells can be further genetically modified to express GLP-1 or its cognate receptor to enhance the glucose responsiveness of the cells (see for example paragraphs [0108 and 0110]). Sharma further proposes that these cells can be used for the treatment of subjects having an insulin-related disorder (see for example paragraph [0114]), thereby suggesting that the cells for treating a subject and the cells for producing insulin are interchangeable in nature. Thus the teachings of Sharma make obvious the use of the human endocrine pancreatic β-cells that recombinantly express PDX-1 and NeuroD/BETA2 for the production of insulin.

However, Sharma does not specifically teach a method wherein the human endocrine pancreatic β-cells that recombinantly express PDX-1 and NeuroD/BETA2 are contacted with a GLP-1 agonist, the co-expression of one or more recombinant oncogenes in those cells, or the co-expression of a telomerase gene in these cells.

Levine also teaches a method of producing insulin in a human endocrine pancreatic β-cells that recombinantly express PDX-1, wherein the cell is additionally contacted with a GLP-1 agonist (see for example the Abstract and column 2, lines 30-37). Levine further contemplates

culturing cells that further express one or more recombinant oncogenes, or alternatively a recombinant telomerase (see for example column 3, lines 7-11). Levine further suggests that these cells should be cultured in contact with other cells in the culture, including as three-dimensional aggregates (se for example column 5, lines 56-58). Additionally, Levine suggests the use of βlox5 cells, specifically, to use as the insulin producing cell background (see for example column 3, lines 1-2). Indeed, the only clear difference between the instantly claimed invention and the invention described in Levine is the inclusion of a recombinant NeuroD/BETA2 gene in the cells that are used for the production of insulin.

It would have been obvious to the ordinary skilled artisan to combine the teachings of Sharma and Levine for the following reasons:

1. Both teachings involve the production of insulin using recombinant human endocrine pancreatic β-cells; specifically, the cells from each teaching comprise PDX-1. Thus, the inventions concern both the same subject matter and are directed toward the same outcomes (the production of insulin) using highly similar tools (the recombinant cells). As a result, it would be obvious to combine the teachings;

2. Sharma clearly recognizes the benefits of using GLP-1 agonists and receptors for the production of insulin (see for example paragraphs [0108] and [0110]) using human endocrine pancreatic β-cells, which is also made obvious by the teachings of Levine; and

3. There is no clear reason as to why the cells taught by Sharma, which additionally overexpress NeuroD/BETA2 would not be applicable in the method set forth by Levine. Indeed, Levine teaches the use of cells comprising a recombinant PDX-1, which encompasses the specific cells taught by Sharma (comprising recombinant PDX-1 and NeuroD/BETA2). As such, it would be

obvious to use the specific cells described by Sharma in the method described by Levine (which makes use of a broad genus of cells that includes those described by Sharma) because Sharma teaches that such cells can be used in methods of producing insulin (such as the one taught by Levine).

The ordinary skilled artisan would have been motivated to combine the teachings because, the combined methods provide potential methodologies to treat prevalent insulin-related diseases such as diabetes (as taught by both Sharma (see for example paragraph [0092]) and Levine (see for example column 4, lines 10-24)), and also because Levine indicates that their teachings result in "powerful tools that should allow identification of the full complement of genes that are required for endocrine cell development and function," and "an opportunity to study how different signal transduction pathways interact with one another to control a complex differentiation program" (see for example column 4, lines 3-9). Thus, absent evidence to the contrary, the ordinary skilled artisan would have had a reasonable expectation of success when combining the teachings of Sharma (regarding the use of a human endocrine pancreatic β-cell to produce insulin) in the method taught by Levine (which involves using a genus of cells, which include those cells described by Sharma, to produce insulin).

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Lambertson, Ph.D.
AU 1636

JAMES KETTER
PRIMARY EXAMINER